THE EFFICACY OF ALPHA-BLOCKERS FOR EXPULSION OF DISTAL URETERAL STONES

Dissertation submitted to

THE TAMILNADU Dr. M.G.R. MEDICAL UNIVERSITY

in partial fulfillment of the

requirements for the award of the degree of

M.Ch. UROLOGY

BRANCH – IV

THE TAMILNADU Dr. M.G.R. MEDICAL UNIVERSITY

CHENNAI, TAMILNADU, INDIA

AUGUST -2009

DECLARATION

I solemnly declare that this dissertation "**The Efficacy of Alpha-Blockers for Expulsion of Distal Ureteral Stones**" was prepared by me in the Department of Urology, Government Madras medical college and Hospital, Chennai under the guidance and supervision of **Prof.R.JEYARAMAN, M.Ch.,** Professor & Head of the Department, Department of urology, Government Madras medical college and Hospital, Chennai. This dissertation is submitted to the TamilNadu Dr.MGR Medical University, Chennai in partial fulfillment of the university requirements for the award of degree of M.ch ., Genitourinary Surgery.

Place: Chennai

Date: **Dr.V.RAVI**

ACKNOWLEDGEMENT

I am very grateful to my teacher and guide **Prof. R. Jeyaraman,** Professor & HOD, Department of Urology, Government Madras Medical College and Hospital, Chennai for his expert guidance and help without which this study would not have been possible.

I sincerely thank **Prof.V.Kamaraj, Prof. RM.Meyyappan,** Additional professor of Urology, Government Madras Medical College, Chennai who gave me encouragement and moral support for the completion of this study

I thank all the Assistant Professors of Department of Urology, Government Madras Medical College, Chennai for their encouragement.

I wish to express my sincere thanks to co-postgraduates, patients and all technical staff of Department of Urology, for their kind co-operation .

I am thankful to the Dean, Government Madras Medical College and Hospital, Chennai for permitting me to carry out this study at Government Madras Medical College and Hospital, Chennai.

CONTENTS

INTRODUCTION

The lifetime prevalence of kidney stone disease is estimated at 1% to 15%, with the probability of having a stone varying according to age, gender, race, and geographic location. Stone disease typically affects adult men more commonly than adult women. By a variety of indicators, including inpatient admissions, outpatient office visits, and emergency department visits, men are affected two to three times more frequently than women (Hiatt et al, 1982 ; Soucie et al, 1994 ; Pearle et al, 2005).[1]

Most stones become symptomatic when they fall into the ureter causing pain or obstruction.

The goal of management of patients suffering from ureteral calculi is to achieve complete stone clearance with minimal attendant morbidity. Treatments for distal ureteric stones include watchful waiting, ESWL, Ureteroscopy and open ureterolithotomy. Although the treatment options available to the urologist are greater now than they have ever been, most patients with ureteral calculi do not require intervention. Ureteral calculi 4 mm or smaller will usually pass spontaneously, although in some cases with discomfort and expense to the patient. Ureteral calculi of any size may be associated with renal

obstruction, and care must be taken to prevent irreversible damage to the kidney, whether the patient selects expectant or active treatment.

Various medications used to enhance the stone passage. It had been demonstrated that α adrenoreceptors antagonists, given to patients suffering from renal colic, due to distal ureterolithiasis, had increased the frequency of stone expulsion rate, reduced the time to expulsion and reduced analgesics consumption.Most of the studies evaluated the efficacy of Tamsulosin, which is a selective α 1A and α 1D adrenoreceptors antagonist. (The lower intramural portion of the ureter, where it passes through the detrusor muscle contains mostly α 1D and α 1A adrenergic receptors)

Only very few studies describe the use of Alfuzosin, which is an α adrenergic receptor blocker and not selective for any α 1 adrenergic receptor, for expulsion of distal ureteric stones.Alfuzosin is a drug with a proven efficacy and considered uroselective with high specificity and sensitivity, for the treatment of BPH.

So, the present study was carried out to evaluate the efficacy of Alpha blockers for expulsion of distal ureteral calculus.

To compare the efficacy of Tamsulosin (Receptor Sub selective Alpha blocker) with Alfuzosin (Receptor non Sub selective Alpha blocker) in the management of distal ureteral calculus.

AIMS & OBJECTIVES

To evaluate the efficacy of Alpha blockers for expulsion of distal ureteric calculus.

To compare the efficacy of Tamsulosin (Receptor Sub Selective Alpha blocker) with Alfuzosin (Receptor non Sub selective Alpha blocker) in the management of distal ureteric calculus.

REVIEW OF LITERATURE

Historical Overview

Ambroise Paré is credited with the first account of ureteral calculi in 1564, as he described “the cruel pain [that] tormented the patient in that place where the stone lodged.” Morris reported in 1898 that “operations on the ureter are an advance of the last few years, but not many have been recorded up to the present time” (Ballenger et al, 1933). In 1910, Gibson of New York described an incision parallel to and just above Poupart's ligament, wholly extraperitoneal, by which the lower ureter, even down to its entrance into the bladder, could be readily exposed. This safe and comparatively easy approach to the ureter placed open ureterolithotomy on sound footing. During the last two decades the management of urteric calculus has changed radically; with advent of ESWL, Endourologic approaches, PCNL, laparoscopy, Medical expulsive therapy has made the open surgery for urinary stones obsolete.

Anatomy of Ureter

The ureters are bilateral tubular structures responsible for transporting urine from the renal pelvis to the bladder. They are

generally 22 to 30 cm in length. The normal ureter is not of uniform caliber, with three distinct narrowings classically described: the ureteropelvic junction, crossing of the iliac vessels, and the ureterovesical junction. These three sites of ureteral narrowing are clinically significant because they are common locations for urinary calculi to lodge during passage..

Ureteral Segmentation and Nomenclature

The ureter can be divided into upper, middle, and lower segments. The upper ureter extends from the renal pelvis to the upper border of the sacrum. The middle ureter comprises the segment from the upper to the lower border of the sacrum. The lower (distal or pelvic) ureter extends from the lower border of the sacrum to the bladder.

Ureteral Innervation

The exact role of the ureteral autonomic input is unclear. Normal ureteral peristalsis does not require outside autonomic input but, rather, originates and is propagated from intrinsic smooth muscle pacemaker sites located in the minor calyces of the renal collecting system. The autonomic nervous system may exert some modulating effect on this process, but the exact role is unclear. The ureter receives preganglionic

sympathetic input from the 10th thoracic through 2nd lumbar spinal segments. Postganglionic fibers arise from several ganglia in the aorticorenal, superior, and inferior hypogastric autonomic plexuses. Parasympathetic input is received from the 2nd through 4th sacral spinal segments.

Role of the Nervous system in ureteral function

The ureter is a syncytial type of smooth muscle without discrete neuromuscular junctions (Burnstock, 1970)[2.] Ureteral peristalsis may persist after transplantation (O'Conor and Dawson-Edwards, 1959)[3] or denervation (Wharton, 1932)[4,] because spontaneous activity may occur in isolated in vitro ureteral segments (Finberg and Peart, 1970)[5,] and because normal ante grade peristalsis continues after reversal of a segment of ureter in situ (Melick et al, 1961)[6], it is apparent that ureteral peristalsis can occur without innervations. However, analysis of the data in the literature clearly indicates that the nervous system plays at least a modulating role in ureteral peristalsis.

Parasympathetic nervous system

Although the role of the parasympathetic nervous system in the control of ureteral peristalsis has not been well defined, muscarinic

cholinergic receptors have been demonstrated in the ureter (Latifpour et al, 1989, 1990)[7].The cholinergic innervation is especially rich in the distal and intravesical ureter (Hernández et al, 1993)[8]

Cholinergic agonists, including ACh, methacholine (Mecholyl), carbamylcholine (carbachol), and bethanechol (Urecholine), in general have been observed to have an excitatory effect on ureteral and renal pelvic function, that is, to increase the frequency and force of contractions (Vereecken, 1973 ; Longrigg, 1974 ; Rose and Gillenwater, 1974 ; Morita et al, 1986, 1987 [260] [259]; Maggi and Giuliani, 1992 ; Hernández et al, 1993 ; Prieto et al, 1994)[9.]

Atropine is a competitive antagonist of the muscarinic effects of ACh. Even when atropine has been observed to inhibit ureteral activity, its effects are frequently minimal and inconsistent (Ross et al, 1967)10, thus providing little rationale for its use in the treatment of ureteral calculus.

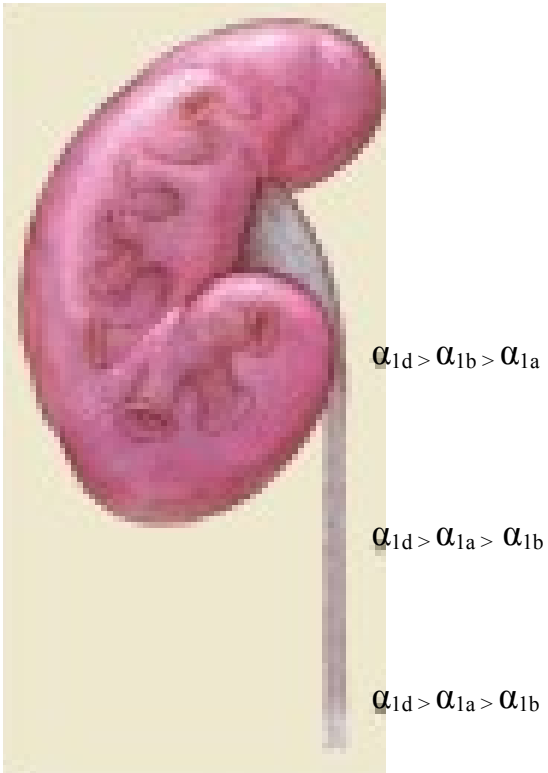
Sympathetic Nervous system

The sympathetic nervous system appears to modulate ureteral activity as evidenced by the demonstration of adrenergic receptors in the ureter (Latifpour et al, 1989, 1990)[7] The ureter contains excitatory α-

adrenergic and inhibitory β-adrenergic receptors (McLeod et al, 1973 ; Rose and Gillenwater, 1974 ; Weiss et al, 1978)[10] that have been demonstrated with receptor-binding techniques (Latifpour et al, 1989, 1990)[7]. Agents that primarily activate α-adrenergic receptors, such as norepinephrine and phenylephrine, tend to stimulate ureteral and renal pelvic activity (McLeod et al, 1973 ; Hernández et al, 1992 ; Rivera et al, 1992 ;)[7] and agents that primarily activate β-adrenergic receptors, such as isoproterenol and orciprenaline, tend to inhibit ureteral and renal pelvic activity (Finberg and Peart, 1970 ; Rose and Gillenwater, 1974 ; Weiss et al, 1978 ; Hernández et al, 1992 ;)[7]

The human ureter contains α-adrenergic receptors along its entire length, with the highest concentration in the distal ureter [11,12] Stimulation of the α receptors increases the force of ureteral contraction and the frequency of ureteral peristalsis, whereas antagonism of the receptors has the opposite effects. Malin and colleagues first demonstrated the presence of α-adrenergic receptors in the human ureter in 1970.Adenergic receptors along the entire length of the ureter, increased tone and frequency of contractions occurs in the ureter when exposed to α-adrenergic agonists[11]

More recently, Sigala and colleagues[12]studied α_1-adrenergic receptor gene and protein expression in the proximal, middle, and distal ureter. They demonstrated that the distal ureter expressed the greatest quantity of α_1 messenger ribonucleic acid (mRNA**). The α_{1d} mRNA was expressed in all portions of the ureter, and it was expressed in significantly greater amounts than the α_{1a} or α_{1b} receptor subtype in both the proximal and distal ureter**. Using ligand binding, they were able to show that the distal ureter had the highest density of α receptors, and α_{1d} was the most common receptor present in all portions of the ureter



There are a number of second messenger intracellular molecules that play a role in the contraction as well as the relaxation of smooth muscle. Cyclic adenosine monophosphate (cAMP) and cyclic guanosine monophosphate (cGMP) modulate relaxation, whereas inositol 1,4,5-triphosphate (IP_3) and diacylglycerol (DG) are involved in contraction. Relaxation occurs after efflux of calcium from the cell and redistribution of this cation within intracellular organelles. The autonomic nervous system is involved in modulation of these events. Parasympathetic activity promotes contraction, whereas sympathetic influences are divergent: α (contraction) and ß (relaxation).

Ureteral Calculi

The factors that the urologist must consider when recommending treatment to patients with ureteral calculi may be grouped into three broad categories: **stone-related factors, clinical factors, and technical factors (equipment available for treatment, costs**). These factors may be thought of as treatment modifiers; the presence or absence of one or more of these factors may shift the balance toward a certain treatment modality.

Factors Affecting Management of Ureteral Stones

Stone Factors	*Clinical Factors*	*Technical Factors*
Location	Symptom severity	Available equipment
Size	Patient's expectations	Cost
Composition	Associated infection	
Degree of obstruction	Solitary kidney	
	Abnormal ureteral anatomy	

Natural History

The indications for intervention in the management of patients with ureteral calculi have clearly been affected by the increased efficiency and lower morbidity of minimally invasive treatment modalities. Although the traditional indications for intervention (intolerable or intractable symptoms, infection, obstruction, and a stone that is unlikely to pass spontaneously) have not changed, the array of technologies currently available allows almost any symptomatic patient to be considered a candidate for stone removal. Many patients will pass the stone spontaneously. A thorough knowledge, then, of the natural history of ureteral stones permits a well-informed judgment of when conservative measures (e.g., observation), rather than intervention, are

indicated. Furthermore, such data help the patient consider the spectrum of options and decide whether to try to endure further symptoms or to elect immediate stone removal.

In the absence of external ureteral compression or internal narrowing, the width of the stone is the most significant measurement affecting the likelihood of stone passage (Ueno et al, 1977)[13.] However, the measurement of stone size from a plain radiograph can be misleading. Otnes and Sandnes (1978)[14] reported that stone size was overestimated in 59% of cases, was underestimated in 15%, and correlated accurately with the actual size in only 26%. Ueno and colleagues (1977)[13] reported that in a series of 520 patients with ureteral stones, **those with stones smaller than 4 mm, 4 to 6 mm, and larger than 6 mm experienced rates of spontaneous passage of 80%, 59%, and 21%, respectively.** Morse and Resnick (1991)[15] showed that **the rate of spontaneous passage is highly dependent on stone location; passage rates from the proximal, middle, and distal ureter were 22%, 46%, and 71%, respectively.** Hubner and associates (1993)[16] also reported that the likelihood of spontaneous stone passage was directly related to stone size and location at the time of presentation. The rate of spontaneous passage for stones smaller than 4 mm was 38% compared

with 1.2% for those larger than 6 mm, irrespective of their position in the ureter at the time of presentation**. Calculi discovered in the distal third of the ureter had a spontaneous passage rate of 45%, compared with 22% for the middle third and 12% for the proximal third.** Two thirds of all stones that passed did so within 4 weeks after the onset of symptoms. Segura and associates (1997)[17] reported in **the AUA guidelines on the management of patients with ureteral calculi that for stones smaller than 5 mm, the spontaneous passage rate in the distal ureter and proximal ureter ranged from 71% to 98% and from 29% to 98%, respectively, whereas stones larger than 5 mm had a lower spontaneous passage rate, ranging from 10% to 53% and 25% to 53% for proximal and distal ureteral calculi, respectivel**y. These rates have been affirmed by a more recent review of CT imaging of ureteral calculi (Coll et al, 2002)[18.] Therefore, **for patients with stones of 5 mm or less, conservative management should be considered,** whereas the chance of spontaneous passage for larger stones diminishes considerably, and intervention should be more readily contemplated.

Miller and Kane (1999)[19] analyzed 75 patients with ureteral calculi and found that the interval to stone passage was highly variable

and dependent on stone size, location, and side: for 95% of stones to pass, 31 days were required for stones 2 mm or less, and about 40 days were required for stones 2 to 6 mm. Furthermore, only 4.8% of patients with stones smaller than 2 mm required intervention compared with 50% of patients with stones 4 to 6 mm. Cummings and coworkers (2000)[20] trained an artificial neural network to predict outcome in patients with ureteral stones with 76% accuracy. The duration of symptoms before initial presentation was the most influential factor, followed by degree of hydronephrosis. The importance of symptom duration was reported by several other authors, who concluded that if significant progress has not occurred after 1 month of observation, intervention is usually required (Ibrahim et al, 1991 ; Hubner et al, 1993 ; Singal and Denstedt, 1997)[21]

Factors Affecting Treatment Decisions

Stone Factors

Location

The location at which the passage of a ureteral stone is arrested is an important factor in assessing the likelihood of spontaneous passage as well as in determining the optimal treatment options and their relative successes. The statistical **probability of spontaneous ureteral stone**

passage is directly related to the distance of the ureter to be traversed and inversely related to stone size. Anatomic location has an important effect on what treatment modality has a higher stone-free rate. In the 1980s, proximal ureteral stones were commonly treated with SWL, whereas distal ureteral stones were treated with ureteroscopy (Sosa et al, 1987)22

Stone Burden

The stone burden, in terms of both size and number, may affect what form of therapy will be the most efficient and confer the highest stone-free rate. The majority of ureteral stones pass spontaneously, especially stones less than 5 mm in diameter, and thus can be treated with expectant management (Kinder et al, 1987 ; Segura et al, 1997)[23] Stones larger than 8 mm, however, are unlikely to pass spontaneously in a timely fashion without causing significant symptoms and possible renal damage from obstruction (Ueno et al, 1977)[13].

Composition

Stone composition, if it is known, is useful information to help discern which treatment strategy may be favored (e.g., SWL for fragile calcium oxalate dihydrate stones or ureteroscopy and intracorporeal

lithotripsy for cystine or brushite stones that are relatively resistant to SWL).

Duration of Presence

The management of patients with ureteral stones may be affected by the duration of a stone's presence or the patient's symptoms. The length of time a stone has been in the ureter is significant because of the potential for irreversible loss of renal function. However, even with complete ureteral obstruction, irreversible loss of renal function does not occur before 2 weeks, although it can progress to total renal unit loss at up to 6 weeks (Vaughan and Gillenwater, 1971)[24] Because the patient's symptoms and stone size do not predict loss of renal function, and because there is no clear time threshold for irreversible damage, intervention should be considered in any patient with ureteral obstruction unless the ability to closely monitor renal function is available**.**

CLINICAL FACTORS

Pain

Pain (renal or ureteral colic) is the primary presenting symptom of most patients with ureteral obstruction and is the source of considerable

morbidity.). Management of ureteral obstruction on the basis of symptoms should be tailored to the amount of time the symptoms have persisted. Patients presenting with early symptoms of renal colic may be managed expectantly for stone passage as long as their symptoms are controllable with oral medical therapy. Patients with symptoms of longer duration may be more appropriately managed by relieving the ureteral obstruction through either the placement of a ureteral stent or definitive stone treatment. Patients with ureteral stones causing severe symptoms refractory to conservative and medical therapy require prompt treatment.

Infection

Infection associated with ureteral stones, or obstructed pyelonephritis, is a not uncommon and potentially life-threatening urologic emergency**.** Such patients are typically febrile and may present with signs of septic shock, such as hypotension. Urgent drainage of the obstructed portion of the urinary tract by either ureteral catheter or percutaneous nephrostomy is essential.

Patient's Expectations

The patient's expectations must be considered in recommending different treatment modalities. For ureteral stones with low probability

of spontaneous passage, the patient must be informed of the available treatments, including the relative benefits and risks associated with each.

Solitary Kidney

Patients with ureteral stones in either surgically or functionally solitary kidneys require a modification of standard treatment algorithms. **A ureteral stone obstructing a solitary kidney demands prompt attention,** usually with internal drainage and definitive stone treatment (ESWL or ureteroscopy).

Aberrant Anatomy

Ureteral stones in patients with abnormal anatomy (ureteral ectopia, ureteroceles, megaureters) may have impaired egress because of obstructive or functional factors (Kajikawa et al, 1985 ; Diamond et al, 1994 ; Dretler, 1995)[25] These patients may not respond to therapies such as SWL with the same level of success as do those with normal ureteral anatomy. The anatomic abnormality may need to be corrected or circumvented to permit successful treatment of ureteral stones. For example, patients with recurrent stones that become lodged and obstruct the ureter in a ureterocele should have the ureterocele treated (by either

endoscopic incision or open excision with reimplantation) simultaneously with ureteral stone removal.

Technical Factors

The treatment of patients with ureteral calculi depends on multiple surgical technologies, and the availability of certain equipment will affect the possible options for treatment. tree model to identify the most cost-effective treatment option for patients with ureteral calculi. On the basis of a comprehensive literature review to determine the average success rate of observation, SWL, and ureteroscopy, they found that ureteroscopy is the most cost-effective treatment strategy for ureteral stones at all locations, after observation fails**.**

Distal Ureteral Calculus

Treatments for distal ureteric calculus include watchful waiting, Extracorporeal shock wave lithotripsy, Ureteroscopy and open ureterolithotomy. If possible,wathful waiting may be considered as the first choice of the treatment because it non invasive and low cost. The optimal therapy for patients requiring removal of distal ureteral calculi is controversial. SWL and ureteroscopy are both effective treatments associated with high success rates and limited morbidity. A 1997 meta-

analysis performed by the AUA Ureteral Stones Clinical Guidelines Panel established that both ureteroscopy and SWL are acceptable treatment options for patients with distal ureteral stones. Both recommended treatment options, SWL and ureteroscopy, have valid advantages and disadvantages. The primary goal in treating patients with ureteral calculi is a stone-free state, and the AUA guidelines panel's meta-analytic study reported that 85% of 9422 patients subjected to SWL were rendered stone free compared with 89% of 3978 patients undergoing ureteroscopy. There have been two randomized prospective studies comparing ureteroscopy and SWL for treatment of patients with distal ureteral stones subsequent to the guidelines document. Peschel and associates (1999)[26] randomized 80 patients and found that those undergoing ureteroscopy achieved stone-free status more rapidly, regardless of initial stone size, than did those treated by SWL. All of the patients undergoing ureteroscopy were rendered stone free, whereas 10% of the SWL cohort required subsequent ureteroscopy to achieve a stone-free status.

There is no validated instrument available to assess the satisfaction of patients for either of these procedures, although this is an important concern. Peschel and associates (1999) measured patients'

satisfaction after ureteroscopy or SWL. They found that for patients with stones smaller than 5 mm, all patients undergoing ureteroscopy reported complete satisfaction, compared with 75% of those undergoing SWL. For those with stones larger than 5 mm, all patients undergoing ureteroscopy were satisfied, compared with 95% of those undergoing SWL. Pearle and associates (2001)[27] also measured patients' satisfaction and found no significant difference between SWL (96%) and ureteroscopy (89%). Neither of these studies used a validated questionnaire, and the divergent conclusions of these two analyses emphasize the need for the development of such a device.

Medical Expulsive Therapy (MET) :

MET has been aimed at modifiable factors that can affect stone passage.These factors are mucosal edema, inflammation, infection, ureteral spasm. Several agents have been studied as potential MET.

Calcium Channel Blockers :

Ureteral smooth muscle contraction is dependent on transcellular and intracellular calcium fluxes. Calculi may induce ureteral spasm that inhibits stone passage. An effective pharmacologic agent would inhibit spasm without significantly impacting ureteral peristalsis because the

latter is thought to promote stone passage. Calcium channel blockers, which inhibit the influx of extracellular calcium, have been prescribed to facilitate stone passage. Nifedipine, verapamil, and diltiazem have been shown to inhibit ureteral contraction in guinea pigs and humans.[28,29,30,31]

Studies suggest that a combination of nifedipine and corticosteroid therapy is effective in facilitating stone passage. Borghi and associates, in a randomized double-blind controlled trial of 86 patients with ureteral stones less than 15 mm in width, demonstrated a statistically significant increased stone expulsion rate for patients given 40 mg nifedipine and 16 mg methylprednisolone daily for a maximum of 45 days than for patients receiving placebo and 16 mg methylprednisolone daily (86% vs 65%). Furthermore, mean time to passage was also statistically significantly less with this regimen than with placebo (11.2 days vs 16.5 days).. Most recently, Porpiglia and colleagues, in a randomized prospective trial, demonstrated the efficacy of nifedipine and deflazacort (an oral steroid) in treating distal ureteral stones ≤ 10 mm in length. The spontaneous passage rate for the control arm (75 mg diclofenac as needed) was statistically significantly lower, 35%, as compared to 79% for the treatment group (30 mg deflazacort daily for up to 10 days, 30 mg nifedipine daily for up to 4 weeks, 75 mg

diclofenac as needed). Mean time to expulsion was also statistically significantly decreased with the treatment arm (7 days vs 20 days) as was average amount of diclofenac used (15 mg vs 105 mg). Serious side effects were minimal, but included transient hypotension and palpitations.[34]

α-Adrenergic Blockers :

Stimulation of α-1 adrenergic receptors enhances contractile frequency and amplitude. A pharmacologic agent that antagonizes the α-1 receptor activity should therefore decrease contractile activity associated with ureteral spasm induced by calculi, thus facilitating passage. There have been reports indicating that the administration of selective α-1 blocking agents facilitates passage of ureteral calculi. Cervenakov and associates, in a nonrandomized study, administered 0.4 mg of tamsulosin, a selective α-1 antagonist, per day to 51 patients with ureteral calculi (mean W 4.0 mm and mean L 7.6 mm) and compared them to a similar number of patients with ureteral stones of similar size (mean W 3.8 mm and mean L 7.5 mm) receiving standard supportive care. Forty-one of the 51 (80.4%) receiving tamsulosin passed their stones spontaneously as compared to 32 (62.8%) in the other cohort. Time to passage was also more expeditious in the tamsulosin group.[37]

A recent randomized controlled trial by Dellabella and associates demonstrated that tamsulosin may be effective in facilitating the passage of distal ureteral calculi. The patients in this study had calculi ranging from 3.8 mm to 13 mm in width. Patients in the treatment group were given oral floroglucinetrimetossibenzene 3 times daily for up to 4 weeks, 30 mg deflazacort daily for 10 days, co-trimoxazole twice daily for 8 days, and 75 mg diclofenac intramuscularly as needed, while the treatment group received 0.4 mg tamsulosin daily for up to 4 weeks with the same dosages of deflazacort, co-trimoxazole, and diclofenac. Passage rates were 70% for the placebo group and 100% for the treatment group. Furthermore, mean hours to expulsion (111.1 vs 65.7), mean number of analgesic injections (2.83 vs 0.13), number of hospitalizations (10 vs 0), and number of stones requiring ureteroscopic intervention (9 vs 0) were all statistically significantly decreased in the treatment group. No drug-related side effects were noted in any of the 60 patients included in the trial.[38] More recently, Dellabella and associates showed, in another randomized controlled trial, that treatment of patients with distal ureteral calculi with tamsulosin was superior to both placebo and nifedipine. All enrolled subjects received 30 mg deflazacort daily for 10 days, co-trimoxazole twice daily for 8 days, and 75 mg diclofenac intramuscularly as needed. The control group received

floroglucinetrimetossibenzene tablets 3 times daily, and the treatment groups received either tamsulosin 0.4 mg daily or 30 mg slow-release nifedipine daily. The group treated with tamsulosin experienced a more statistically significant increase in passage rates than both the control and nifedipine groups (97.1% vs 65.7% and 75.6%, respectively). Furthermore, a statistically significant decrease in time to passage, lower analgesic requirement, decrease in work days lost, and decrease in hospitalization and need for endoscopic stone removal were also demonstrated for the group treated with tamsulosin.[39] Terazosin, another selective α-1 adrenergic antagonist, has also recently been shown to facilitate stone passage. Tekin and colleagues, in a prospective randomized trial of 75 patients with distal ureteral calculi ≤ 15 mm in width, found that patients treated with 5 mg terazosin daily for 4 weeks had a more statistically significant increase in stone passage rate than those patients receiving no treatment (77% vs 46%). Treatment with terazosin was particularly effective for stones < 8 mm, as a statistically significant increase in passage rate was noticed for this subgroup (95% vs 56%). Drug-related side effects were minimal and no patient dropped out of the study.[40]

Tamsulosin : Tamsulosin hydrochloride is an antagonist of alpha1 A adrenoceptors. Tamsulosin is a once-daily administered α_1 antagonist that exhibits some modest degree of selectivity for the α_1a versus the α_1b AR and no selectivity for the α_1a versus the α_1d AR (Foglar et al, 1995). Available in 0.4 mg, 0.8 mg forms. It is administered after a meal, once daily dose. The pharmacokinetic and pharmacodynamic interactions between Tamsulosin and other alpha-adrenergic blocking agents have not been determined. However, interactions may be expected and Tamsulosin should not be used in combination with other alpha-adrenergic blocking agents. Tamsulosin should be used with caution in combination with cimetidine and with moderate or strong inhibitors of CYP2D6 (e.g., fluoxetine) or CYP3A4 (e.g., ketoconazole), particularly at doses higher than 0.4 mg.

Adverse events were generally mild and included dizziness, rhinitis, and abnormal ejaculation. These increased in a dose-dependent manner (increased with 0.8-mg/day dosage than in 0.4 mg/day). Tamsulosin is contraindicated in patients known to be hypersensitive to tamsulosin hydrochloride. Tamsulosin is not indicated in Pregnant, Lactating women, and also in children.

Alfuzosin: Alfuzosin hydro chloride is another α-adrenergic blocking agent that has been extensively utilized in BPH pharmacotherapy. **A**lfuzosin exhibits no pharmacologic uroselectivity for any of the α_1 subtypes (Andersson et al, 1997). alfuzosin should be taken immediately following a meal. Available in 10 mg **A**lfuzosin should not be used in patients with moderate or severe hepatic insufficiency, since alfuzosin blood levels are increased in these patients.

Alfuzosin should not be co-administered with potent CYP3A4 inhibitors such as ketoconazole, itraconazole, and ritonavir, since alfuzosin blood levels are increased.. Alfuzosin contraindicated in patients known to be hypersensitive to Alfuzosin hydrochloride. Tamsulosin is not indicated in Pregnant, Lactating women,and also in children.

Nonsteroidal Anti-Inflammatory Drugs :

In vitro studies of the human ureter have demonstrated that prostaglandins increase ureteral smooth muscle contractility.[41,42] Nonsteroidal anti-inflammatory drug (NSAID) agents that inhibit cyclooxygenase (COX), an enzyme involved in prostaglandin synthesis

from fatty acids, have been used extensively in the management of patients with renal colic. Their benefits are based on various mechanisms including a reduction in RBF that decreases pressure in the collecting system, ureteral smooth muscle relaxation, and a decrease in stone-induced ureteral edema. The latter 2 effects of NSAIDs have been hypothesized to facilitate stone passage as well. Two randomized controlled trials have assessed the ability of NSAIDs to facilitate stone passage. Kapoor and colleagues demonstrated that patients receiving indomethacin suppositories (a nonselective COX inhibitor) did not experience increased stone passage rates or decreased time to passage when compared to patients receiving placebo. However, the patients receiving indomethacin did require a statistically significantly decreased amount of narcotic analgesics.[43] Laerum and associates showed that oral diclofenac, a nonselective COX inhibitor, did not increase stone expulsion rate compared to placebo. However, diclofenac significantly decreased pain and hospital admissions.[44]

Progesterone :

The increased prevalence of hydro-ureteronephrosis beginning during the second trimester of gestation and ending within 1 month postpartum suggests that progesterone and/or estrogen may affect

ureteral function. It has been proposed that progesterone promotes ureteral dilatation during pregnancy and delays the rate of its disappearance postpartum. Mikkelsen and colleages treated 24 patients of both genders with a 250 mg intramuscular dose of hydroxyprogesterone to see if this would facilitate stone passage. Fourteen patients (59%) passed calculi while all other patients required surgical removal.[45] However, the efficacy of this approach cannot be determined as there was no control group.

Future Direction of Pharmacotherapy

COX-2 Inhibitors :

The aforementioned studies suggest that nonselective COX inhibitors are not effective in facilitating stone passage. However, COX-2 inhibitors have not been assessed in this setting. These may prove to be effective agents to facilitate stone passage. Nakada and associates have found that the COX-2 protein and its mRNA are expressed to a greater degree in obstructed human ureter as compared to normal human ureter.[46] Furthermore, this group demonstrated that a selective COX-2 inhibitor reduced the contractility of both human and swine ureter.[46,47]

Phosphodiesterase Inhibitors :

The second messengers, cAMP and cGMP, are mediators of smooth muscle relaxation. cAMP and cGMP breakdown occurs via the activity of a family of isoenzymes known as the phosphodiesterases. Phosphodiesterase (PDE) inhibitors are a class of drugs that inhibit the breakdown of cAMP and cGMP, enhancing smooth muscle relaxation. Therefore, PDE inhibitors may be able to decrease ureteral spasm and facilitate stone passage.[49] Taher and colleagues identified the isoenzyme PDE IV as being dominant over other PDEs in regulation of ureteral smooth muscle.[50] Rolipram, a selective PDE IV inhibitor, has been shown to facilitate ureteral relaxation. Kühn and associates assessed the ability of sodium nitroprusside and various PDE inhibitors to promote relaxation of explanted human ureter. They found that sodium nitroprusside and rolipram were the most effective in promoting ureteral relaxation of the agents tested. Most recently, Romics and colleagues, in a randomized doubleblinded controlled trial, showed that drotaverine, a selective PDE IV inhibitor, significantly reduced acute renal colic when compared to placebo.[52] Although no studies have evaluated PDE

inhibitors as agents to facilitate stone passage, the aforementioned properties suggest that this should be investigated.

Various clinical trials MET

Series	*Therapy*	*No. patients*	*Mean stone size (mm)*	*Stone location*	*Stone passage rate (%)*
Mikkelsen et al (1988)[30]	IM hydroxyprogesterone (no control)	24	Not reported	Any	59
Ahmad et al (1991)[31]	Diclofenac sodium (no control)	80	≤5.0	Any	57.5
Laerum et al (1995)[32]	Diclofenac sodium *v* placebo	41 39	Not reported	Any	68 *v* 74
Borghi et al (1994)[23]	Nifedipine + methylprednisolone *v* placebo + methylprednisolone	43 each	6.7 *v* 6.8	Any	87 *v* 65
Porpiglia et al (2000)[24]	Nifedipine + deflazacort *v* watchful waiting	48 each	5.8 *v* ≤5.5	Distal	79 *v* 35
Saita et al (2004)[33]	Nifedipine + prednisolone *v* prednisolone	25 each	12.0 *v* 12.8	Any	81 *v* 68
Cervenakov et al (2002)[36]	Tamsulosin *v* control	51 each	<10.0	Distal	80 *v* 63
Dellabella et al (2003)[37]	Tamsulosin + deflazacort *v* floroglucine-trimetossibenzene + deflazacort	30 each	6.7 *v* 5.8	Distal	100 *v* 70
Porpiglia et al (2004)[34]	Tamsulosin + deflazacort *v* nifedipine + deflazacort *v* control	28 *v* 30 *v* 28	4.7 *v* 5.4 *v* 5.4	Distal	85 *v* 80 *v* 43
Dellabella et al (2005)[35]	Tamsulosin + deflazacort *v* nifedipine + deflazacort *v* control	70 each	7.2 *v* 6.2 *v* 6.2	Distal	97 *v* 77 *v* 64
Yilmaz et al (2005)[39]	Tamsulosin + deflazacort *v* terazosin *v* doxazosin *v* control	28 *v* 28 *v* 29 *v* 28	6.0 *v* 6.0 *v* 5.9 *v* 6.1	Distal	79 *v* 79 *v* 76 *v* 54
Porpiglia et al (2006)[38]	Tamsulosin *v* deflazacort *v* tamsulosin + deflazacort *v* control	33 *v* 24 *v* 33 *v* 24	6.0 *v* 5.8 *v* 5.9 *v* 5.7	Distal	60 *v* 37.5 *v* 85 *v* 33

AUA Guidelines regarding management of distal urteric calculus :

The index patient is a nonpregnant adult with a unilateral noncystine/nonuric acid radiopaque ureteral stone without renal calculi requiring therapy whose contralateral kidney functions normally and whose medical condition, body habitus, and anatomy allow any one of the treatment options to be undertaken.

Treatment Guidelines for the Index Patient

For Ureteral Stones <10 mm

Option: In a patient who has a newly diagnosed ureteral stone <10 mm and whose symptoms are controlled, observation with periodic evaluation is an option for initial treatment. Such patients may be offered an appropriate medical therapy to facilitate stone passage during the observation period.

[Based on review of the data and panel opinion/Level 1A]

The Panel performed a meta-analysis of studies in which spontaneous ureteral stone passage was assessed. The median probability of stone passage was 68% for stones ≤5 mm (n=224) and 47% for those >5 and ≤10 mm (n=104) in size (details previously discussed and provided in the appendixes). The Panel recognized that these studies had certain limitations including non standardization of the

stone size measurement methods and lack of analysis of stone position, stone-passage history, and time to stone passage in some. A meta-analysis of MET was also performed which demonstrated that alpha nblockers facilitate stone passage and that the positive impact of nifedipine is marginal. This analysis also indicates that alpha blockers are superior to nifedipine and, hence, may be the preferred agents for MET (details provided in the Appendixes). A similar benefit of MET was demonstrated in a recently published meta-analytic study.7. The majority of stones pass spontaneously within four to six weeks. This was demonstrated by Miller and Kane8, who reported that of stones ≤2 mm, 2 to 4 mm and 4 to 6 mm in size, 95% of those which passed did so by 31, 40, and 39 days, respectively. In a choice between active stone removal and conservative treatment with MET, it is important to take into account all individual circumstances that may affect treatment decisions. A prerequisite for MET is that the patient is reasonably comfortable with that therapeutic approach and that there is no obvious advantage of immediate active stone removal.

Standard: Patients should be counseled on the attendant risks of MET including associated drug side effects and should be informed that it is administered for an "off label" use.

[Based on Panel consensus/Level IV]

Standard: Patients who elect for an attempt at spontaneous passage or MET] should have well-controlled pain, no clinical evidence of sepsis, and adequate renal functional reserve.

[Based on Panel consensus/Level IV]

Standard: Patients should be followed with periodic imaging studies to monitor stone position and to assess for hydronephrosis.

[Based on Panel consensus/Level IV]

Standard: Stone removal is indicated in the presence of persistent obstruction, failure of stone progression, or in the presence of increasing or unremitting colic.

[Based on Panel consensus/Level IV]

For Ureteral Stones >10 mm

Although patients with ureteral stones >10 mm could be observed or treated with MET, in most cases such stones will require surgical treatment. No recommendation can be made for spontaneous passage (with or without medical therapy) for patients with large stones.

For Patients Requiring Stone Removal

Standard: A patient must be informed about the existing active treatment modalities, including the relative benefits and risks associated with each modality.

[Based on Panel consensus/Level IV]

Specifically, both SWL and URS should be discussed as initial treatment options for the majority of cases.

Recommendation: For patients requiring stone removal, both SWL and URS are acceptable first-line treatments.

[Based on review of the data and Panel consensus/Level 1A-IV.The meta-analysis demonstrated that URS yields significantly greater stone-free rates for the majority of stone stratifications.

Option: Laparoscopic or open surgical stone removal may be considered in rare cases where SWL, URS, and percutaneous URS fail or are unlikely to be successful.

[Based on Panel consensus/Level III]

The 1997 AUA guideline stated that "Open surgery should not be the first-line treatment." The invasiveness and morbidity of open surgery can be avoided. In very difficult situations, however, such as with very large, impacted stones and/or multiple ureteral stones, or in cases of concurrent conditions requiring surgery, an alternative procedure might be desired as primary or salvage therapy. Laparoscopic ureterolithotomy is a less invasive alternative to open surgery in this setting.

Recommendations for the Nonindex Patient.

Standard: For septic patients with obstructing stones, urgent decompression of the collecting system with either percutaneous drainage or ureteral stenting is indicated. Definitive treatment of the stone should be delayed until sepsis is resolved.

[Based on Panel consensus/Level III]

Medical Expulsive Therapy[53]

There is growing evidence that MET, the administration of drugs to facilitate stone passage, can be efficacious. Studies have demonstrated that this approach may facilitate and accelerate the spontaneous passage of ureteral stones as well as stone fragments

generated with SWL.34-38 Our meta-analysis demonstrated the effectiveness of MET. Nine percent (CI: -7% to 25%) more patients receiving nifedipine passed their stones than did controls in our meta-analysis, a difference that was not statistically significant. In contrast, a statistically significant 29% (CI: 20% to 37%) more patients passed their stones with alpha blocker therapy than did control patients. These findings indicate that alpha blockers facilitate ureteral stone passage while nifedipine may provide a marginal benefit. Therefore, the Panel feels that alpha blockers are the preferred agents for MET at this time. Similar findings have been reported by Hollingsworth and associates, who recently performed a meta-analysis of studies involving alpha blockers or nifedipine in patients with ureteral stones. The differences in methodology from our study have been previously mentioned. Patients given either one of these agents had a greater likelihood of stone passage than those not receiving such therapy. The pooled-risk ratios and 95% CIs for alpha blockers and calcium channel blockers were 1.54. The benefit of adding corticosteroids was reported to be small. Tamsulosin has been the most common alpha blocker utilized in these studies. However, one small study demonstrated tamsulosin, terazosin, and doxazosin as equally effective in this setting. These studies also demonstrated that MET reduces the stone passage time and limits pain.

The beneficial effects of these drugs are likely attributed to ureteral smooth muscle relaxation mediated through either inhibition of calcium channel pumps or alpha-1 receptor blockade. Further prospective and randomized studies are warranted to determine the patients who best respond to MET.

MATERIALS & METHODS

All the patients who presented to the Urological Department in the period between January 2007 to January 2009 with history suggestive of ureteric colic were evaluated for inclusion in the study

- Informed consent obtained from all the patients.
- Patients were segregated into 3 groups.
- The investigator knew the patients in each of the groups before the start of the intervention, but the Patients didn't.
- All details regarding patients demographics, Investigations, Outcome and complications were entered into the proforma.

Type of the study: Prospective Cohort study with control

Initial Evaluation

All the patients who presented with history suggestive of ureteric colic were evaluated with

History &Physical Examination

Urinalysis &Urine culture Sensitivity

Complete Blood Count

Renal Function Test

USG KUB &X –ray KUB

Calculus size was measured based on X-ray KUB

X-ray KUB was taken initially, 28 days or after the calculus passed

Inclusion criteria

Renal colic due to radiologically proven distal ureteric calculus

Exclusion criteria :

Stone larger than 10 mm

Urosepsis

Additional calculus that might be the reason for the renal colic

Severe hydronephrosis

Known sensitivity to α blockers

Concomitant treatment with α blockers, β blockers, calcium Antagonist, nitrates

Pregnancy

Inability to provide informed consent

Previous of surgery or endoscopic procedures in the urinary tract

History of spontaneous stone expulsion

Known ureteral stricture

Patients were segregated into 3 groups

A Group Patients were given Placebo

B Group Patients were given Tamsulosin 0.4 mg/day

C Group Patients were given Alfuzosin 10 mg/day

Analgesics 100 mg SR tablets were given on demand

Duration of treatment – Until stone passage but not more than 4wks

Primary endpoint of the study:

Calculus passage.

Discontinuation of treatment:

1. Intractable pain

2. Complications

   (i) Urosepsis

   (ii) Drug related complication

Following Factors were analyzed:

Age

Sex

Calculus passage rate -Stone size

Calculus passage time –Stone size

Patients requiring intervention

Reason for intervention

Analgesics requirements

Statistical Analysis were done using SPSS

Chi-Square Test

Multiple range test -Turkey –HSD Test

Levene's Test for equality of variance

RESULTS & OBSERVATION

Total number of the patients 150. Patients were segregated into 3 groups.50 patients were allotted in each groups

Age Stratification

Table 1 - Age Stratification

Age groups	Group A	Group B	Group C
15-20	9(18%)	7(14%)	8(16%)
21-30	24(48%)	26(52%)	33(66%0
31-40	11(22%)	12(24%)	8(!6%)
41-50	6(12%)	5(10%)	1(2%)

p = 0.44

Mean age of the patients in Group A 27.0 years (range between18- 45 years), Group B 26.8 years (range between 18- 45 years) and in Group C 25.4 years (range between 18-41 years). Majority of the patients found to be in the age group of 21-30 years. Age distribution in all the 3 groups were found to be similar

Sex Stratification

Table 2 - Sex Stratification

Sex	Group A	Group B	Group C
Male	31(62%)	30(60%)	31(62%)
Female	19(38%)	20(40%)	19(38%)

p = 0. 97

In all the 3 groups Male and Female patients were distributed in equal proportions.

Side Stratification

Table 3 - Side Stratification

Side	Group A	Group B	Group C
Right	24(48%)	24(48%)	19(38%)
Left	26(52%)	26(52%)	31(62%0

p = 0.5

There was no side predominance in any of the groups.

Calculus Size Stratification

Table 4 : Calculus Size Stratification

Calculus size	Group A	Group B	Group C

4mm	7	11	6
5mm	3	8	6
6mm	3	6	6
7mm	18	8	14
8mm	11	12	10
9mm	8	5	8

p = 0.1382

Mean calculus size in Group A 6.98 mm (range between 4-9mm), in Group B 6.34mm (range between 4-9mm) and in Group C 6.78mm (range between4-9mm).The stone size was found to be equally distributed in all the groups.

Colicky pain stratification

Table 5 : Duration of Pain

Groups	Mean	Range
A	1.8 days	1-4 days
B	1.7 days	1-4 days

C	1.8days	1-5 days

Patients had colicky pain for about 1.8 days before presentation duration ranged from (1-5 days).

Outcome stratification

Table 6 : Calculus Expulsion Rate

Groups	Expulsion	Failure	Total
A	16(32%)	34(68%)	50(100%)
B	36(72%)	14(28%)	50(100%)
C	37(74%)	13(26%)	50(100%)

p=0.00001

Calculus expulsion rate in Group A, Group B and in Group C were found to be 32%,72%,74% respectively. Difference were statistically significant.

Table 7 : Expulsion of Calculus in relation to Stone Size

Calculus size	Group A		Group B		Group C	
	Expulsion	Failure	Expulsion	Failure	Expulsion	Failure

≤6mm	11	2	24	1	17	1
> 6mm	5	32	12	13	20	12

p = 0.000001 p = 0.00016 p = 0.013

Only 4/56 (7.1%) cases had failures in ≤ 6mm groups, compared with 57/94 (60.6%) in > 6mm groups. This difference had high statistical significance in all the groups.

Expulsion time stratification

Table 8 : Expulsion time in relation to treatments

Groups	**No of days of treatment**
A	8.63 ± 3.24 days
B	7.75 ± 3.14 days
C	8.57 ± 4.52 days

p = 0.5961

There was no statistical significance in calculus expulsion time in all the 3 groups.

Expulsion time stratification - calculus size ≤ 6 mm

Table 9 : Expulsion time of calculus size ≤ 6 mm

Groups	No of days of treatment
A	7.36 ± 2.91
B	6.50 ± 2.50
C	5.53 ± 1.23

P =0.1155

There was no statistical significance in expulsion time of calculus ≤ 6mm in all the 3 groups.

Expulsion time stratification - calculus size > 6 mm

Table 10 : Expulsion time of calculus size > 6 mm

Groups	No of days of treatment
A	11.40 ± 2.07
B	10.25 ±2.83
C	11.15 ± 4.70

p =0.7844

There was no statistical significance in expulsion time of calculus >6mm in all the 3 groups.

Intervention requirement (URS)

Table 11 : Intervention requirement

Groups	No of cases
A	34 (68%)
B	14(28%)
C	13(26%)

p= 0.00001

Intervention requirement (URS) in Group A, Group B and in Group C were found to be 68%,28%,26% respectively. Difference were statistically significant.

Intervention requirement (URS) based on calculus size

Table 12 : Intervention requirement in relation to calculus size

Calculus size	**Group A**	**Group B**	**Group C**
≤ 6mm	2 (15.4%)	1(4%)	1(5.6%)
>6mm	32(86.5%)	13(52%)	12(37.5%)
p value	0.00001	0.00016	0.0134

Intervention requirement in ≤ 6mm calculus in the Group A, Group B and in Group C were 15.4%, 4%, 5.6% respectively. Intervention requirement in > 6mm calculus in the Group A, Group B and in Group C were 86.5%, 52%,37.5% respectively This difference had high statistical significance in all the groups.

Analgesic Requirements

Table 13 : Analgesic Requirements

Groups	No. of doses of analgesic requirement
A	6.60 ± 1.82
B	3.86 ± 2.51
C	4.18 ± 3.02

p =0.03

The analgesic requirement was more in the placebo groups mean duration of more than 6 dose.

DISCUSSION

150 Patients were included in the study. Patient were categorized into 3 groups. A Group Patients were given Placebo, B Group Patients were given Tamsulosin 0.4 mg/day and C Group Patients were given Alfuzosin 10 mg/day. Analgesics 100 mg SR tablets were given on demand.Each group comprised of 50 patients.Mean age group of the patient were in Placebo (Group A) 27.0 years (range between18- 45 years), Tamsulosin (Group B) 26.8 years (range between 18- 45 years) and in Alfuzosin (Group C) 25.4 years (range between 18-41 years). Majority of the patients found to be in the age group of 21-30 years. Age distribution in all the 3 groups were found to be similar. Male :Female ratio in Placebo (GroupA), Tamsulosin (Group B) and in Alfuzosin (Group C) found to be 1.6:1,1.5 :1,1.6:1 respectively. Right side :Left side ratio in Placebo (GroupA), Tamsulosin (Group B) and in Alfuzosin (Group C) found to be 1.08:1,1.08 :1,1.6:1 respectively. Mean calculus size were in Placebo (6.98± 1.6 mm).in Tamsulosin (6.34± 1.7mm) and in Alfuzosin (6.7± 1.5 mm). The size of calculus were found to be equally distributed in all 3 groups. Patients had colicky pain for about 1.8 days before presentation, duration ranged in between (1-5 days)

Table 14 : Comparison of various parameters

Variable	Group A	Group B	Group C	Statistical significance
No of Pts	50	50	50	
Age (years)	27±7.3	26.7± 7.4	25.4± 5.2	NS
SEX M:F	1.6:1	1.5:1	1.6:1	NS
Side R:L	1.08: 1	1.08:1	1.6:1	NS
Stone size mm	6.98± 1.6	6.34± 1.7	6.7± 1.5	NS
Expulsion rate	32%	72%	74%	0.00001
Expulsion Time days	8.63 ± 3.24	7.75 ± 3.14	8.57 ± 4.52	NS
Ureteroscopy	68%	28%	26%	0.00001
Analgesic requirements (doses)	6.60 ± 1.82	3.86 ± 2.51	4.18 ± 3.02	0.03

In Placebo (Group A) Patients 16/50 (32%) of calculus found to be expelled and 34/50 (68%) patients required interventions, In Tamsulosin (GroupB) Patients 36/50 (62%)of calculus found to be expelled and 14/50 (28%) patients required interventions. In Alfuzosin (Group C) Patients 37/50 (74%) of calculus found to be expelled and

13/50 (26%) patients required interventions. Calculus expulsion rate in Placebo, Tamsulosin and in Alfuzosin were 32%, 72%,74% respectively

Multivariate analysis

Table 15 : Significance of variation among three groups

Variables	Group A & Group B	Group A & Group C	Group B & Group C
Age	NS	NS	NS
Stone size	NS	NS	NS
Expulsion rate	0.00006	0.00003	NS
Expulsion time	NS	NS	NS
Ureteroscopy	0.00002	0.00005	NS

There was a statistically significant difference in calculus expulsion rate in between Placebo (Group A) & Tamsulosin (Group B) patients and in between Placebo (Group A) & Alfuzosin (Group C) patients. (This results are comparable with other studies) but there was no significant difference between Tamsulosin (Group B) & Alfuzosin (Group C) patients, so receptor sub selectivity is not a major concern. Only 4/56 (7.1%) cases had failures in ≤ 6mm groups, compared with 57/94 (60.6%) in > 6mm groups.

Table 16 : Distal Ureteral Stone Expulsion Rate (%)

Study	With Alpha Blocker	Without Alpha Blocker	p Value
Cervenakov et al	80.4	62.8	N/A
Dellabella et al	100	70	0.001
Resim et al	86.6	73.3	0.196
De Sio et al	90	58.7	0.01
Yilmaz et al	79.31 (Tamsulosin) 78.57 (Terazosin) 75.86 (Doxazosin)	53.57 53.57 53.57	0.03 0.03 0.03
Porpiglia et al	85	43	< 0.001
Dellabella et al	97.1	64.3	<0.0001
This study	72 (Tamsulosin) 74 (Alfuzosin)	32	0.00001

This difference had high statistical significance in all the groups [(Placebo) p value = 0.000001, (Tamsulosin) p = 0.00016, (Alfuzosin) p = 0.013] Calculus expulsion time were found to be in Placebo Group A(8.63 ± 3.24 days), in Tamsulosin Group B (7.75 ± 3.14 days) and in Group C (8.57 ± 4.52 days). There was no statistically significant

difference found in between the groups. There was no statistical significance in expulsion time of calculus size of ≤ 6mm and in > 6 mm in all the 3 groups. Analgesics requirements was more in the placebo groups, mean duration was more than 6 days. 61/150 of patients required ureteroscopy &Lithotripsy [Placebo (Group A) 34 (68%), Tamsulosin Group B 14(28%), Alfuzosin Group C 13(26%)]. Reason for intervention were found to be intractable pain in 51 patients, Non Expulsion of calculus in 9 patients and due to dizziness (Adverse effect of Tamsulosuin) in 1 patient. Interventions were found to be more in the Placebo Group A patients [34 (68%)]. Discontinuation of the treatment due to side effect of the drug is almost negligible. No patients complained of retrograde ejaculation, which may be due to short duration of treatment and or a possible decrease or absence of coitus due to ureteric colic.

CONCLUSION

- Alpha blockers (Tamsulosin, Alfuzosin) improve the spontaneous expulsion rate of distal ureteric calculus.

- There is no difference in distal ureteric calculus expulsion rate between Tamsulosin, and Alfuzosin.

- Alpha blockers reduce the analgesic requirements but not the calculus expulsion time.

BIBLIOGRAPHY

1. Hiatt et al., 1982. Hiatt RA, Dales LG, Friedman GD, Hunkeler EM: Frequency of urolithiasis in a prepaid medical care program. *Am J Epidemiol* 1982; 115:255-265. Higashihara et al., 1984. Higashihara E, Nutahara

2. Burnstock et al., 1972. Burnstock G, Satchell DG, Smythe A: A comparison of the excitatory and inhibitory effects of non-adrenergic, non-cholinergic nerve stimulation and exogenously applied ATP on a variety of smooth muscle preparations from different vertebrate species. *Br J Pharmacol* 1972; 46:234.

3. O'Conor and Dawson-Edwards, 1959. O'Conor Jr VJ, Dawson-Edwards P: Role of the ureter in renal transplantation. I: Studies of denervated ureter with particular reference to ureteroureteral anastomosis. *J Urol* 1959; 82:566.

4. Wharton, 1932. Wharton LR: The innervation of the ureter, with respect to denervation. *J Urol* 1932; 28:639.

5. Finberg and Peart, 1970. Finberg JPM, Peart WS: Function of smooth muscle of the rat renal pelvis—Response of the isolated pelvis

muscle to angiotensin and some other substances. *Br J Pharmacol* 1970; 39:373.

6. Melick et al., 1966. Melick WF, Brodeur AE, Herbig F, Naryka JJ: Use of a ureteral pacemaker in the treatment of ureteral reflux. *J Urol* 1966; 95:184.

Melick et al., 1961. Melick WF, Naryka JJ, Schmidt JH: Experimental studies of ureteral peristaltic patterns in the pig. II. Myogenic activity of the pig ureter. *J Urol* 1961; 86:46.

7. Latifpour et al., 1990. Latifpour J, Kondo S, O'Hollaren B, et al: Autonomic receptors in urinary tract: Sex and age differences. *J Pharmacol Exp Ther* 1990; 253:661.

Latifpour et al., 1989. Latifpour J, Morita T, O'Hollaren B, et al: Characterization of autonomic receptors in neonatal urinary tract smooth muscle. *Dev Pharmacol Ther* 1989;

8. Hernández et al., 1993. Hernández M, Simonsen U, Prieto D, et al: Different muscarinic receptor subtypes mediating the phasic activity and basal tone of pig isolated intravesical ureter. *Br J Pharmacol* 1993; 110:1413.

9. Prieto et al., 1994. Prieto D, Simonsen U, Martín J, et al: Histochemical and functional evidence for a cholinergic innervation of the equine ureter. *J Auton Nerv Syst* 1994; 47:159

10, Ross et al., 1967. Ross JA, Edmond P, Griffiths JM: The action of drugs on the intact human ureter. *Br J Urol* 1967; 39:26.

11. Malin JM, Deane RF, Boyarsky S. Characterisation of adrenergic receptors in human ureter. *Br J Urol.* 1970;42:171–174. [PubMed]

12. Sigala S, Dellabella M, Milanese G, et al. Evidence for the presence of alpha1 adrenoceptor subtypes in the human ureter. *Neurourol Urodynamics.* 2005;24:142–148.

13. Ueno et al., 1977. Ueno A, Kawamura T, Ogawa A, et al: Relation of spontaneous passage of ureteral calculi to size. *Urology* 1977; 10:544-546.

14. Otnes and Sandnes, 1978. Otnes B, Sandnes H: Comparison of radiological measurement and actual size of ureteral calculi. *Scand J Urol Nephrol* 1978; 12:155-156.

15. Morse and Resnick, 1991. Morse RM, Resnick MI: Ureteral calculi: natural history and treatment in an era of advanced technology. *J Urol* 1991; 145:263-265.

16. Hubner and Porpaczy, 1990. Hubner W, Porpaczy P: Treatment of caliceal calculi. *Br J Urol* 1990; 66:9-11.

Hubner et al., 1993. Hubner WA, Irby P, Stoller ML: Natural history and current concepts for the treatment of small ureteral calculi. *Eur Urol* 1993; 24:172-176

17. Segura et al., 1997. Segura JW, Preminger GM, Assimos DG, et al: Ureteral Stones Clinical Guidelines Panel summary report on the management of ureteral calculi. The American Urological Association. *J Urol* 1997; 158:1915-1921.

18. Coll et al., 2002. Coll DM, Varanelli MJ, Smith RC, et al: Relationship of spontaneous passage of ureteral calculi to stone size and location as revealed by unenhanced helical CT. *AJR Am J Roentgenol* 2002; 178:101-103.

19. Miller and Kane, 1999. Miller OF, Kane CJ: Time to stone passage for observed ureteral calculi: A guide for patient education. *J Urol* 1999; 162(pt 1):688-690.discussion 690-691

20. Cummings et al., 2000. Cummings JM, Boullier JA, Izenberg SD, et al: Prediction of spontaneous ureteral calculous passage by an artificial neural network. *J Urol* 2000; 164:326-328.

21. Ibrahim et al., 1991. Ibrahim AI, Shetty SD, Awad RM, et al: Prognostic factors in the conservative treatment of ureteric stones. *Br J Urol* 1991; 67:358-361.

22. Sosa et al., 1987. Sosa RE, Riehle RA, Vaughan Jr ED: The management of ureteral calculi. *Semin Urol* 1987; 5:212-216.

23. Kinder et al., 1987. Kinder RB, Osborn DE, Flynn JT, et al: Ureteroscopy and ureteric calculi: How useful?. *Br J Urol* 1987; 60:506-508.

24. Vaughan and Gillenwater, 1971. Vaughan Jr ED, Gillenwater JY: Recovery following complete chronic unilateral ureteral occlusion: Functional, radiographic and pathologic alterations. *J Urol* 1971; 106:27.

25. Kajikawa et al., 1985. Kajikawa H, Kameoka H, Nishimoto N, et al: Ectopic ureteral opening in four males: Including a case of inverted Y ureteral duplication [in Japanese]. *Hinyokika Kiyo* 1985; 31:2039-2048.

26. Peschel et al., 1999. Peschel R, Janetschek G, Bartsch G: Extracorporeal shock wave lithotripsy versus ureteroscopy for distal ureteral calculi: A prospective randomized study. *J Urol* 1999; 162:1909-1912.

27. Pearle et al., 2001. Pearle MS, Nadler R, Bercowsky E, et al: Prospective randomized trial comparing shock wave lithotripsy and ureteroscopy for management of distal ureteral calculi. *J Urol* 2001; 166:1255-1260.

28 Golenhofen K, Lammel E. Selective suppression of some components of spontaneous activity in various types of smooth muscle by iproveratril (Verapamil). *Pfleugers Arch.* 1972;331:233–243.

29 Forman A, Andersson KE, Henriksson I, et al. Effects of nifedipine on the smooth muscle of the human urinary tract in vitro and in vivo. *Acta Pharmacol Toxicol (Copenh).* 1978;43:111–118.

30. Hertle L, Nawrath H. Calcium channel blockade in smooth muscle of the human upper urinary tract. I. Effects on depolarization-induced activation. *J Urol.* 1984;132:1265–1269.

31. Hertle L, Nawrath H. Calcium channel blockade in smooth muscle of the human upper urinary tract. II. Effects on norepinephrine-induced activation. *J Urol.* 1984;132:1270–1274.

32. Borghi L, Meschi T, Amato F, et al. Nifedipine and methylprednisolone in facilitating ureteral stone passage: a randomized, double-blind, placebo-controlled study. *J Urol.* 1994;152:1095–1098.

33. Cooper JT, Stack GM, Cooper TP. Intensive medical management of ureteral calculi. *Urology.* 2000;56:575–578.

34. Porpiglia F, Destefanis P, Fiori C, Fontana D. Effectiveness of nifedipine and deflazacort in the management of distal ureter stones. *Urology.* 2000;56:579–582.

35. Peters HJ, Eckstein W. Possible pharmacological means of treating renal colic. *Urol Res.* 1975;4:55–59.

36. Lindsey D, Parker DA, Arganese T, et al. Modification by dipyrone (noramidopyrine methanesulphonate) of stone-induced ureteric hyperperistalsis in the dog. *Urol Res.* 1979;7:13–17

37. Cervenakov I, Fillo J, Mardiak J, et al. Speedy elimination of ureterolithiasis in lower part of ureters with the alpha 1-blocker—tamsulosin. *Int Urol Nephrol.* 2002;34:25–29.

38. Dellabella M, Milanese G, Muzzonigro G. Efficacy of tamsulosin in the medical management of juxtavesical ureteral stones. *J Urol.* 2003;170:2202–2205.

39. Dellabella M, Milanese G, Muzzonigro G. The medical-expulsive therapy for distal ureteral stones: which is the optimal choice [abstract]? *J Urol.* 2004;171(Suppl):1151.

40. Tekin A, Alkan E, Beysel M, et al. Alpha-1 receptor blocking therapy for lower ureteral stones: a randomized prospective trial [abstract]. *J Urol.* 2004;171(Suppl):1152. Abstract.

41. Cole RS, Fry CH, Shuttleworth KED. The action of the prostaglandins on isolated human ureteric smooth muscle. *Br J Urol.* 1988;61:19–26.

42. Zwergel U, Zwergel T, Ziegler M. Effects of prostaglandins and prostaglandin synthetase inhibitors on acutely obstructed kidneys in the dog. *Urol Int.* 1991;47:64–69.]

43. Kapoor DA, Weitzel S, Mowad JJ, et al. Use of indomethacin suppositories in the prophylaxis of recurrent ureteral colic. *J Urol.* 1989;142:1428–1430.]

44. Laerum E, Ommundsen OE, Gronseth JE, et al. Oral diclofenac in the prophylactic treatment of recurrent renal colic. *Eur Urol.* 1995;28:108–111.

45. Mikkelsen AL, Meyhoff HH, Lindahl F, Christensen J. The effect of hydroxyprogesterone on ureteral stones. *Int Urol Nephrol.* 1988;20:257–260.

46. Nakada SY, Jerde TJ, Jacobson LM, et al. Cyclooxygenase-2 expression is up-regulated in obstructed human ureter. *J Urol.* 2002;168:1226–1229.

47. Nakada SY, Jerde TJ, Bjorling DE, Saban R. Selective cyclooxygenase-2 inhibitors reduce ureteral contraction in vitro: a better alternative for renal colic? *J Urol.* 2000;163:607–612.

48. Becker AJ, Stief CG, Meyer M, et al. The effect of the specific phosphodiesterase-IV-inhibitor rolipram on the ureteral peristalsis of the rabbit in vitro and in vivo. *J Urol.* 1998;160:920–925.

49. Gruber CM. The effect of morphine and papaverine upon the peristaltic and antiperistaltic contractions of the ureter. *J Pharmacol Exp Ther.* 1928;33:191.

50. Taher A, Schul-Knappe P, Meyer M, et al. Characterization of cyclic nucleotide phosphodiesterase isoenzymes in the human ureter and their functional role in vitro. *World J Urol.* 1994;12:286–291.

51. Kühn R, Ückert S, Stief CG, et al. Relaxation of human ureteral smooth muscle in vitro by modulation of cyclic nucleotide-dependent pathways. *Urol Res.* 2000;28:110–115.

52. Romics I, Molnár DL, Timberg G, et al. The effect of drotaverine hydrochloride in acute colicky pain caused by renal and ureteric stones. *BJU Int.* 2003;92:92–96.

53. AUA Guideline for the Management of Ureteral Calculi 2007

Figure 1 : Right Distal Ureteric Calculus

Figure 2 : Left Distal Ureteric Calculus

Figure 3 : Age Stratification

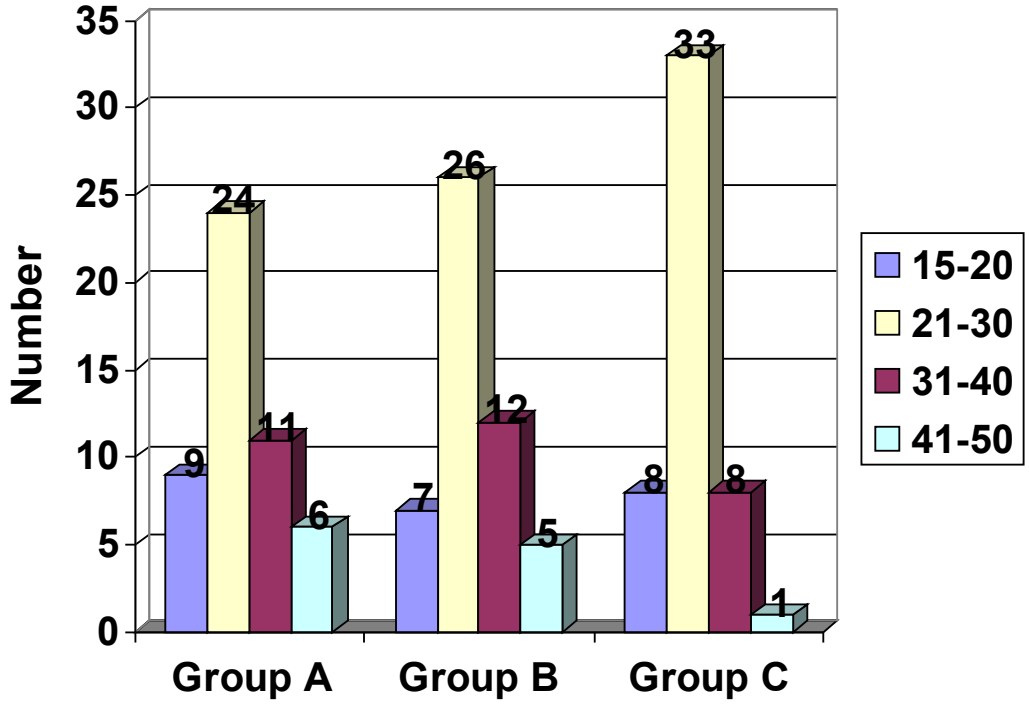


Figure 4 : Sex Distribution

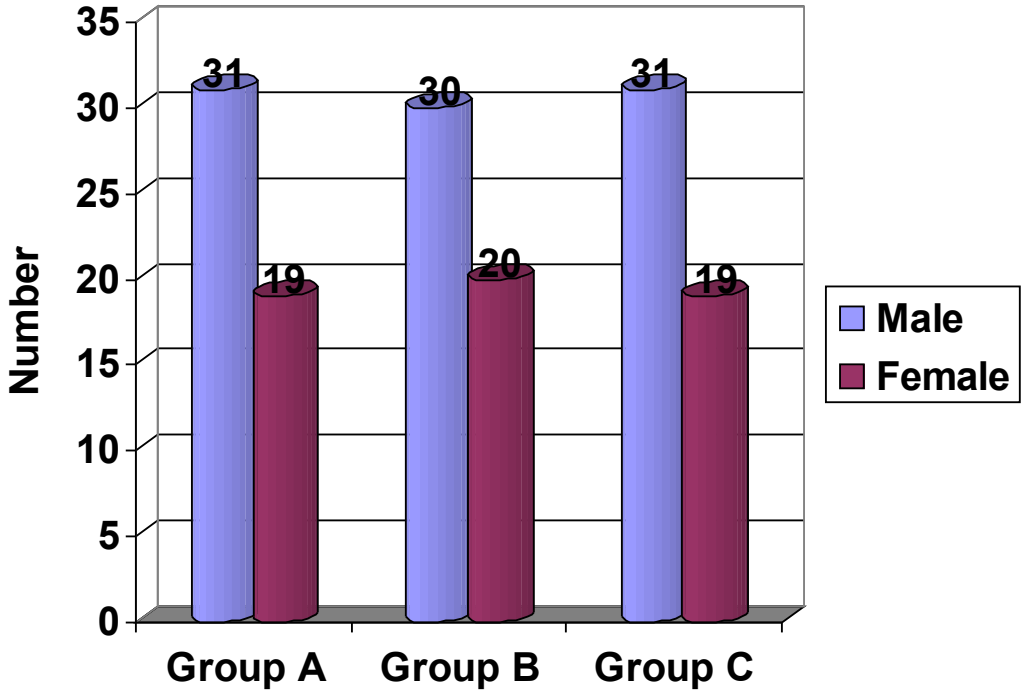


Figure 5 : Side Distribution

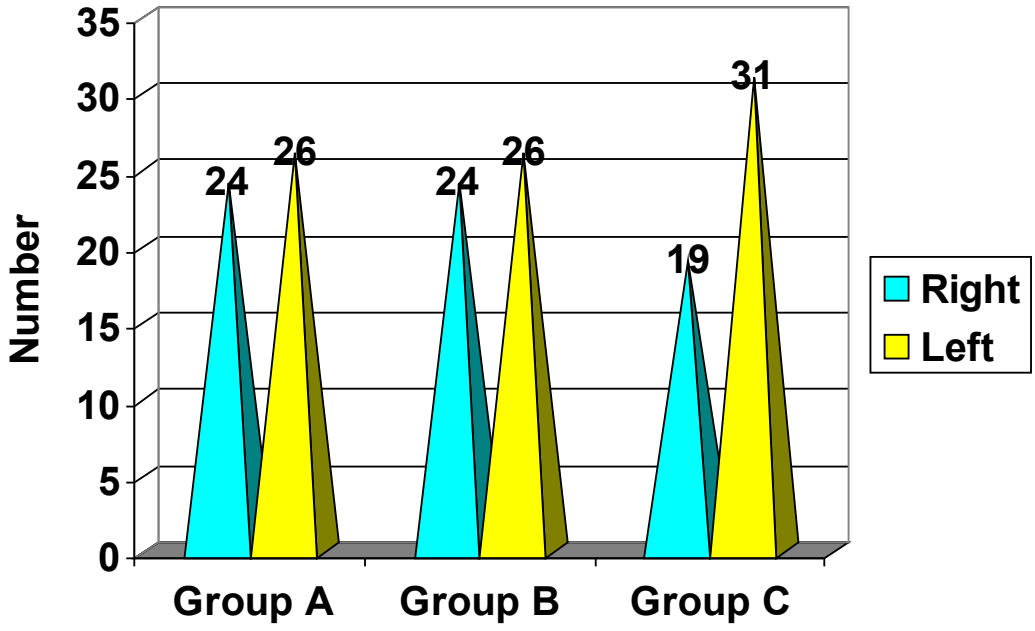


Figure 6 : Calculus size distribution

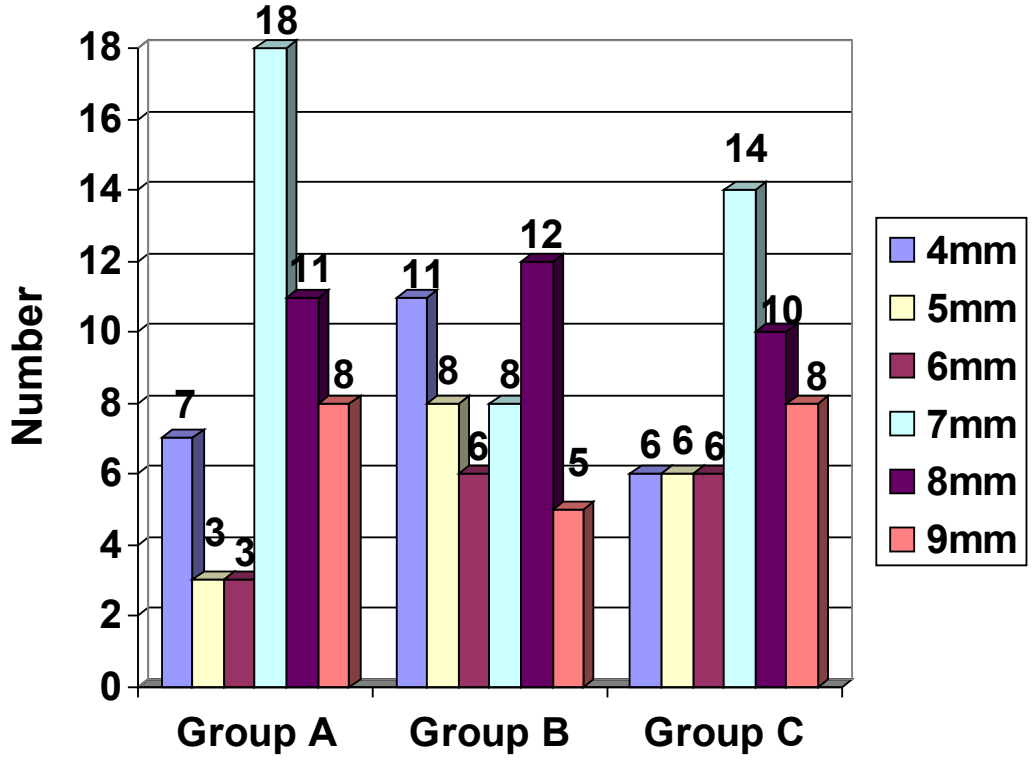


Figure 7 : Outcome

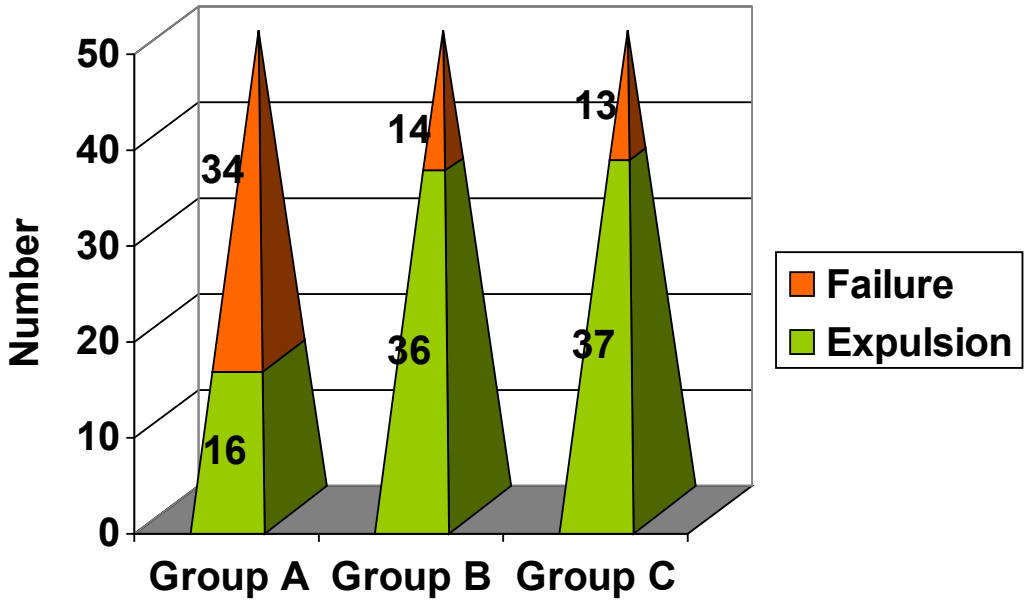
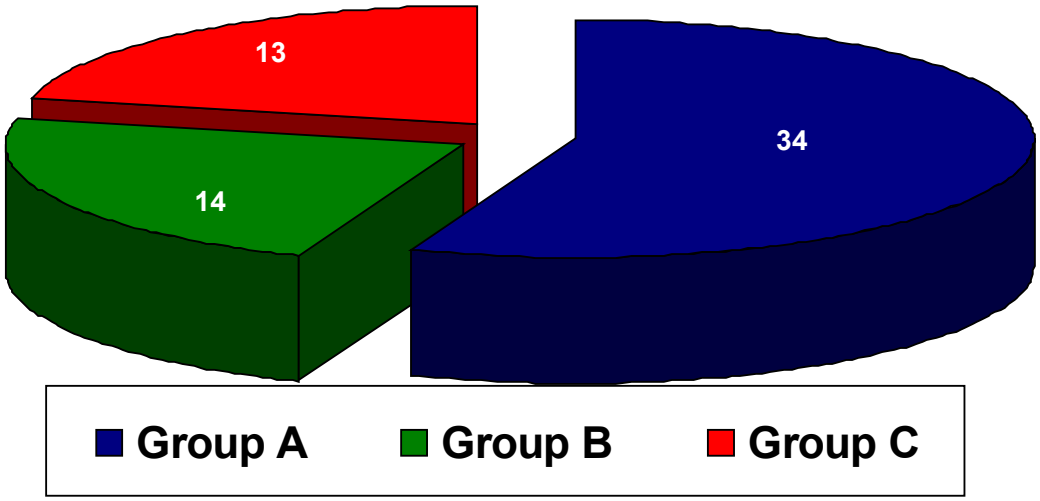


Figure 8 : Intervention



MASTER CHART

NO	Pt.Id	Age	Sex	Side	Colicy	Calculus size	Outcome	Noof days	Analgesic	INV	REV
					Pain	Size			Require		
1	A1	22	M	Lt	2	5	E	7	4	NO	
2	B1	18	M	Lt	1	6	E	5	2	NO	
3	C1	23	M	Lt	2	5	E	7	0	NO	
4	A2	20	F	Rt	2	7	F	10	4	URS	Pain
5	B2	32	F	Rt	3	8	E	5	3	NO	
6	C2	24	M	Lt	2	5	E	8	3	NO	
7	A3	42	M	Lt	1	4	E	5	2	NO	
8	B3	23	F	Lt	1	7	E	10	5	NO	
9	C3	31	F	Rt	2	7	F	12	2	URS	Pain
10	A4	23	M	Lt	3	4	E	7	2	NO	
11	B4	21	M	Rt	1	8	E	11	4	NO	
12	C4	31	M	Lt	1	9	E	18	6	NO	
13	A5	21	F	Lt	2	9	F	10	5	URS	Pain
14	B5	35	F	Lt	2	5	E	5	2	NO	
15	C5	30	M	Lt	1	7	E	10	3	NO	
16	A6	41	M	Rt	2	8	F	28	12	URS	NEC
17	B6	21	F	Rt	1	4	E	5	0	NO	
18	C6	20	M	Lt	3	7	F	20	7	URS	Pain
19	A7	32	M	Lt	2	8	F	15	6	URS	Pain
20	B7	21	F	Rt	3	9	F	20	5	URS	Pain
21	C7	23	M	Lt	2	7	E	9	6	NO	
22	A8	21	F	Lt	2	4	E	5	0	NO	
23	B8	23	M	Lt	1	7	E	9	6	NO	
24	C8	21	F	Lt	2	9	F	20	15	URS	Pain
25	A9	20	M	Rt	1	8	F	28	5	URS	NEC
26	B9	30	M	Rt	3	7	E	10	3	NO	
27	C9	25	F	Lt	1	9	F	10	5	URS	Pain
28	A10	24	M	Lt	2	5	E	12	3	NO	
29	B10	18	M	Lt	3	6	E	5	2	NO	
30	C10	21	M	Rt	1	8	E	11	4	NO	
31	A11	20	F	Rt	1	8	F	7	3	URS	Pain
32	B11	27	M	Lt	1	8	F	20	11	URS	ADE
33	C11	28	F	Lt	2	4	E	5	0	NO	
34	A12	45	F	Lt	1	7	F	11	7	URS	Pain
35	B12	33	M	Rt	2	5	E	3	1	NO	
36	C12	30	F	Lt	1	9	F	11	5	URS	Pain
37	A13	33	M	Rt	2	8	F	28	5	URS	Pain
38	B13	28	F	Rt	1	7	E	11	5	NO	

NO	Pt.Id	Age	Sex	Side	Colicy	Calculus size	Outcome	Noof days	Analgesic	INV	REV
					Pain	Size			Require		
1	A1	22	M	Lt	2	5	E	7	4	NO	
39	C13	25	M	Rt	1	8	E	5	3	NO	
40	A14	31	M	Lt	1	4	E	5	2	NO	
41	B14	28	M	Lt	1	6	E	5	2	NO	
42	C14	20	F	Rt	2	4	E	7	3	NO	
43	A15	31	M	Rt	2	6	F	15	10	URS	Pain
44	B15	22	M	Rt	3	5	E	7	4	NO	
45	C15	18	M	Lt	1	6	E	5	2	NO	
46	A16	23	M	Lt	2	7	F	11	10	URS	Pain
47	B16	20	F	Rt	1	7	F	10	4	URS	Pain
48	C16	32	F	Rt	1	8	E	5	3	NO	
49	A17	24	M	Rt	2	7	F	12	3	URS	Pain
50	B17	42	M	Lt	1	4	E	5	2	NO	
51	C17	23	F	Rt	2	7	E	15	5	NO	
52	A18	31	F	Lt	1	7	F	20	2	URS	Pain
53	B18	23	M	Lt	2	4	E	7	2	NO	
54	C18	21	M	Lt	1	8	E	11	4	NO	
55	A19	31	M	Rt	2	9	F	25	6	URS	Pain
56	B19	21	F	Lt	1	9	F	10	5	URS	Pain
57	C19	35	F	Rt	2	5	E	5	2	NO	
58	A20	30	M	Lt	1	7	E	10	3	NO	
59	B20	41	M	Rt	3	8	F	28	5	URS	NEC
60	C20	21	F	Lt	1	4	E	5	0	NO	
61	A21	20	M	Lt	2	7	F	20	7	URS	Pain
62	B21	32	M	Rt	3	8	E	15	6	NO	
63	C21	21	F	Lt	3	9	F	20	5	URS	Pain
64	A22	23	M	Rt	3	7	F	9	6	URS	Pain
65	B22	21	F	Lt	1	4	E	5	0	NO	
66	C22	23	M	Rt	2	7	E	9	6	NO	
67	A23	21	F	Lt	1	9	F	20	5	URS	Pain
68	B23	20	M	Lt	4	8	F	28	5	URS	NEC
69	C23	30	M	Rt	1	7	E	10	3	NO	
70	A24	25	F	Rt	2	9	F	10	5	URS	Pain
71	B24	24	M	Lt	1	5	E	12	3	NO	
72	C24	18	M	Rt	3	6	E	5	2	NO	
73	A25	21	M	Lt	1	8	F	11	4	URS	Pain
74	B25	20	F	Rt	2	4	E	7	3	NO	
75	C25	27	M	Lt	1	8	F	20	11	URS	Pain
76	A26	28	F	Rt	2	4	E	5	0	NO	
77	B26	45	F	Lt	3	5	E	11	7	NO	

NO	Pt.Id	Age	Sex	Side	Colicy	Calculus size	Outcome	Noof days	Analgesic	INV	REV
					Pain	Size			Require		
1	A1	22	M	Lt	2	5	E	7	4	NO	
78	C26	33	M	Rt	1	5	E	3	1	NO	
79	A27	30	F	Lt	2	9	F	11	5	URS	Pain
80	B27	33	M	Rt	1	8	F	28	5	URS	NEC
81	C27	28	F	Lt	2	7	E	15	5	NO	
82	A28	33	M	Rt	2	7	F	5	5	URS	Pain
83	B28	31	M	Lt	1	4	E	5	2	NO	
84	C28	28	M	Rt	2	6	E	5	2	NO	
85	A29	20	F	Lt	1`	6	F	7	3	URS	Pain
86	B29	31	M	Rt	2	6	F	15	10	URS	Pain
87	C29	30	M	Lt	1	6	E	7	3	NO	
88	A30	41	M	Lt	2	8	F	28	5	URS	Pain
89	B30	21	F	Rt	1	4	E	5	0	NO	
90	C30	20	M	Lt	2	7	F	20	7	URS	Pain
91	A31	32	M	Rt	1	8	F	15	6	URS	Pain
92	B31	21	F	Lt	2	9	F	20	5	URS	Pain
93	C31	23	M	Rt	1	7	E	9	6	NO	
94	A32	21	F	Lt	2	4	E	5	0	NO	
95	B32	23	M	Lt	1	7	E	9	6	NO	
96	C32	21	F	Rt	2	9	F	20	5	URS	Pain
97	A33	20	M	Lt	1	8	F	28	5	URS	NEC
98	B33	30	M	Rt	2	7	E	10	3	NO	
99	C33	25	F	Lt	1	9	F	10	5	URS	Pain
100	A34	24	M	Lt	2	6	E	12	3	NO	
101	B34	18	M	Rt	1	6	E	5	2	NO	
102	C34	21	M	Rt	1	8	E	11	4	NO	
103	A35	20	F	Lt	1	4	E	7	3	NO	
104	B35	27	M	Rt	2	8	F	20	11	URS	Pain
105	C35	28	F	Lt	3	4	E	5	0	NO	
106	A36	45	F	Lt	4	5	E	11	7	NO	
107	B36	42	M	Rt	2	4	E	5	2	NO	
108	C36	23	F	Lt	2	7	E	15	5	NO	
10	A37	31	F	Rt	2	7	F	20	2	URS	Pain

NO	Pt.Id	Age	Sex	Side	Colicy	Calculus size	Outcome	Noof days	Analgesic	INV	REV
					Pain	Size			Require		
1	A1	22	M	Lt	2	5	E	7	4	NO	
9											
110	B37	23	M	Lt	1	4	E	7	2	NO	
111	C37	21	M	Lt	1	8	E	11	4	NO	
112	A38	31	M	Rt	1	9	F	25	6	URS	Pain
113	B38	21	F	Lt	1	9	F	10	5	URS	Pain
114	C38	35	F	Lt	3	5	E	5	2	NO	
115	A39	30	M	Rt	1	7	E	10	3	NO	
116	B39	41	M	Lt	1	8	F	28	5	URS	NEC
117	C39	21	F	Rt	4	4	E	5	0	NO	
118	A40	20	M	Lt	1	7	F	20	7	URS	Pain
119	B40	32	M	Rt	1	8	E	15	6	NO	
120	C40	20	F	Lt	1	5	E	7	3	NO	
121	A41	21	M	Rt	2	7	E	11	5	NO	
122	B41	22	M	Lt	2	6	E	7	3	NO	
123	C41	24	M	Rt	2	8	E	5	10	NO	
124	A42	23	M	Lt	3	7	F	15	10	URS	Pain
125	B42	31	M	Rt	1	8	E	7	3	NO	
126	C42	30	M	Lt	3	7	E	10	3	NO	
127	A43	21	F	Rt	2	9	F	10	5	URS	Pain
128	B43	22	M	Lt	2	5	E	12	3	NO	
129	C43	18	M	Rt	1	6	E	5	2	NO	
130	A44	20	M	Lt	1	8	F	11	4	URS	Pain

NO	Pt.Id	Age	Sex	Side	Colicy	Calculus size	Outcome	Noof days	Analgesic	INV	REV
					Pain	Size			Require		
1	A1	22	M	Lt	2	5	E	7	4	NO	
131	B44	19	F	Lt	1	4	E	7	3	NO	
132	C44	23	M	Rt	1	8	F	20	11	URS	Pain
133	A45	25	F	Rt	2	7	F	5	0	URS	Pain
134	B45	40	F	Lt	2	5	E	11	7	NO	
135	C45	41	M	Lt	2	4	E	5	2	NO	
136	A46	25	F	Rt	3	7	E	15	5	NO	
137	B46	23	F	Lt	2	7	F	20	2	URS	Pain
138	C46	33	M	Lt	1	6	F	7	2	URS	Pain
139	A47	22	M	Rt	2	8	E	11	4	NO	
140	B47	21	M	Lt	1	8	E	11	4	NO	
141	C47	31	M	Lt	5	9	E	25	6	NO	
142	A48	21	F	Rt	4	9	F	10	5	URS	Pain
143	B48	35	F	Rt	1	5	E	5	2	NO	
144	C48	30	M	Lt	2	7	E	10	3	NO	
145	A49	41	M	Rt	2	8	F	28	5	URS	NEC
146	B49	21	F	Rt	1	4	E	5	0	NO	
147	C49	20	M	Lt	2	7	F	20	7	URS	NEC
148	A50	32	M	Rt	2	8	F	15	6	URS	Pain
149	B50	21	F	Rt	2	9	F	20	5	URS	Pain
150	C50	23	M	Lt	2	7	E	9	6	NO	

A- Placebo, B-Tamsulosin C-Alfuzosin M-Male F-Female

Rt - Right, Lt- left, E- Expelled , F-Failure , INV-Intervention

NEC- Non Expulsion of calculus, ADE – Adverse Effect

REV - Reasons for intervention

PATIENT CONSENT FORM

Study Title **: The Efficacy of Alpha-Blockers for Expulsion of Distal Ureteral Stones**

Study Centre **: Department of Urology**

Patient's Name :

Patient's Age :

Identification No :

Patients may tick these Boxes [ ]

I confirm that I have understood the purpose of procedure for the above study. [ ]

I have the opportunity to ask the questions and all my questions and doubts have been answered to my complete satisfaction. [ ]

I understand that my participation in the study is voluntary and that I am free to withdraw at any time without giving any reason, without my legal right being affected [ ]

I understand that sponsor of the clinical study, others working on the sponsor's behalf, the ethics committee and the regulatory authorities will not need my permission to look at my health records both in respect of the current study and any further research that may be conducted in relation to it, even if I withdraw from study. [ ]

I agree to this access, however, I understand that my identity would not be revealed. In any information released to third parties or published, unless as required under the law. [ ]

I agree not to restrict the use of any data or results that arise from this study. [ ]

I agree to take part in the above study and to comply with the instructions given during the study and to faithfully to cooperate with the study team, and to immediately inform the study staff if I suffer from any deterioration in my health or my well being or any unexpected or unusual symptoms. [ ]

I hereby give consent to participate in this study. [ ]

Signature / Thumb Impression ..... of the patient:

Place : .....
Patient's name and address : .....
Signature of the Investigator :.....Place .....Date .....
Name of the Investigator : .....

PATIENT PROFORMA

Name: **Address:**

Age: **Sex:** **I.P/O.P No:**

I.D.No :

Complaints:

Physical Examination:

B/P - **mm/Hg**

Investigations:

Urinalysis: **Albumin:**

Sugar:

Deposit: **Pus cells :**

RBC:

Urine culture /sensitivity:

Total count: **P:** **E:** **L:** **M:**

Hb: **PCV:**

X –ray KUB:

Side: **Size of calculus:**

IVU:

USG:

RK **LK**

Size:

PCS:

CMD:

Treatment Given:

TREATMENT OUTCOME*:*

Calculus passed : **Yes:** **No:**

If passed: **Size:**
Time:

Analgesic requirement:

If not passed: **Intervention details :**

Complications: